DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

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WARNING LETTER
VIA EXPRESS

AUG 6 2001

Mr. Giuseppe Vignati
Owner, President & Managing Director
Diffuplast SRL
Via Piave, 48
Olgiate Olona, 21057, Italy

Dear Mr. Vignati:

During an inspection of your firm located in Olgiate Olona, Italy on June 19-21, 2001, our investigator determined that your firm manufactures parenteral and enteral nutritional bags. These products are devices as defined by Section 201(h) of the Federal, Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation, as specified in Title 21, Code of Federal Regulation (CFR), Part 820, as follows:

1. Failure to establish and maintain procedures for implementing corrective and preventive action, which include requirements for verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example:

   a. There is no requirement to validate changes, when needed, to ensure that such actions are effective and do not adversely affect the product.
   b. A report of non-conformity was received on March 26, 2001 regarding the QA testing of the plastic bag used to hold the parenteral feeding bag during administration. The contract specification developer stated the test [redacted] was inadequate to evaluate the side seams of the bag, which was verified by Diffuplast. The QA procedure recommended by Diffuplast was changed to include the use [redacted] instead of the [redacted] There was no verification or validation to ensure the corrective action was effective and did not adversely affect the use of the product.

2. Failure to establish and maintain adequate procedures for finished device acceptance and release to ensure that each production run, lot, or batch of finished device meets acceptance criteria, as required by 21 CFR 820.80(d). For example:

a. The parenteral and enteral bags manufactured by Diffuplast are marked with graduations indicating liquid capacity, which are not checked or tested for accuracy. It is maintained that these graduations are approximate but the labeling does not indicate they are approximate measures.

b. As a common practice, sterilization lots are released prior to receiving the hard copy certification of sterility.

3. Failure to establish and maintain procedures to control the design of the device, in order to ensure that specified design requirements are met, as required by 21 CFR 820.30(a)(1). For example, no design control procedures have been established or maintained.

4. Failure to adequately establish with a high degree of assurance a process which cannot be verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example, the biological indicators are not assayed before use in any of the sterilization validations performed at Diffuplast.

In addition to the above GMP observations, the following Medical Device Reporting cite was observed:

1. Failure to develop, maintain, and implement written Medical Device Reporting procedures, as required by 21 CFR 803.17. For example, your firm had no knowledge of Medical Device Reporting.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Given the serious nature of these violations of the Act, it may be recommended to our Office of Regulatory Affairs that all shipments of parenteral and enteral nutritional bags manufactured by Diffuplast SRL of Olgiate Olona, Italy be placed on Detention Without Physical Examination until these violations are corrected.

In order to remove the devices from this Detention Without Physical Examination, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. We acknowledge your July 6, 2001 response to the FDA 483. Review of your response indicates that you have adequately addressed item 3.b. of the FDA 483; however, all other items on the FDA 483 remain unaddressed.

After we notify you that you have submitted an adequate response, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections have been verified, your products may resume entry into this country.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make correction to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If documentation is not in English, please provide an English translation to facilitate our review. Please address your response and any questions to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement II, General Hospital Devices Branch, HFZ-333, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Ms. Carolyn Niebauer.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Ms. Leslie E. Dorsey at the letterhead address or at 301.594.4618 or FAX 301.594.4638.

Sincerely yours,

Larry Spears
Acting Director
Office of Compliance
Center for Devices and Radiological Health